Application of stem cells derived from the periodontal ligament or gingival tissue sources for tendon tissue regeneration.

Journal: Biomaterials

Publication Year: 2014

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PubMed link: 24397989

Funding Grants: CIRM Stem Cell Biology Training Program

Public Summary:
Here, we sought to establish dental-derived MSCs as a population of MSCs that can be used in applications where the regeneration of tendon tissue is desired. Therefore, one of our primary objectives was to determine the plasticity of these MSCs in this regenerative mode at an ectopic site.

Scientific Abstract:
Tendon injuries are often associated with significant dysfunction and disability due to tendinous tissue's very limited self-repair capacity and propensity for scar formation. Dental-derived mesenchymal stem cells (MSCs) in combination with appropriate scaffold material present an alternative therapeutic option for tendon repair/regeneration that may be advantageous compared to other current treatment modalities. The MSC delivery vehicle is the principal determinant for successful implementation of MSC-mediated regenerative therapies. In the current study, a co-delivery system based on TGF-beta3-loaded RGD-coupled alginate microspheres was developed for encapsulating periodontal ligament stem cells (PDLSCs) or gingival mesenchymal stem cells (GMSCs). The capacity of encapsulated dental MSCs to differentiate into tendon tissue was investigated in vitro and in vivo. Encapsulated dental-derived MSCs were transplanted subcutaneously into immunocompromised mice. Our results revealed that after 4 weeks of differentiation in vitro, PDLSCs and GMSCs as well as the positive control human bone marrow mesenchymal stem cells (hBMMSCs) exhibited high levels of mRNA expression for gene markers related to tendon regeneration (Scx, DCn, Tnmd, and Bgy) via qPCR measurement. In a corresponding in vivo animal model, ectopic neo-tendon regeneration was observed in subcutaneous transplanted MSC-alginate constructs, as confirmed by histological and immunohistochemical staining for protein markers specific for tendons. Interestingly, in our quantitative PCR and in vivo histomorphometric analyses, PDLSCs showed significantly greater capacity for tendon regeneration than GMSCs or hBMMSCs ($P < 0.05$). Altogether, these findings indicate that periodontal ligament and gingival tissues can be considered as suitable stem cell sources for tendon engineering. PDLSCs and GMSCs encapsulated in TGF-beta3-loaded RGD-modified alginate microspheres are promising candidates for tendon regeneration.